March 7, 2017

Since 2003, NHGRI has celebrated 'National DNA Day' on April 25 to commemorate the successful completion of the Human Genome Project in 2003 and the discovery of DNA's double-helical structure in 1953. This annual event offers students, teachers, and the public many exciting opportunities to learn about the latest advances in genetics and genomics, and to explore how those advances may influence their lives. I would like to take this opportunity to urge you to get involved in this annual celebration by encouraging your local STEM education and outreach programs to host a National DNA Day event in your area. Check out genome.gov/105063670 for more information.

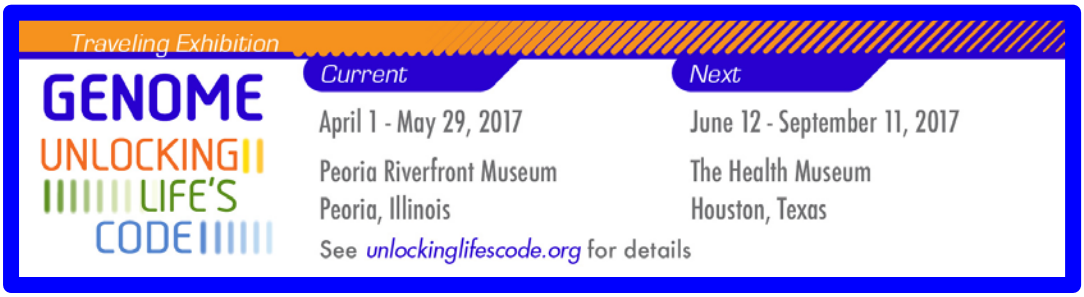
In addition, I call your attention to a recent Request for Information (RFI) soliciting feedback on the data-submission and data-access processes associated with the database of Genotypes and Phenotypes (dbGaP). This is part of broader efforts to enhance and streamline management of data under the NIH Genomic Data Sharing Policy. I encourage researchers who use dbGaP to submit their feedback. For additional information, see genome.gov/27567918.

This month's *The Genomics Landscape* features stories about:

- Rare Disease Research at NHGRI: Not So Rare
- New Secretary of Health and Human Services
- UDN Publishes Framework for Diagnosing Rare Diseases
- ENCODE Team 'Spills All'
- Guide to Interpreting Genomic Reports: A Genomics Toolkit

All the best,

Watch here for current and upcoming locations of the Smithsonian-NHGRI exhibition "Genome: Unlocking Life's Code" as it tours North America!



~To manage your subscription to *The Genomics Landscape*, see: list.nih.gov/cgi-bin/wa.exe?A0=NHGRILANDSCAPE~
~To suggest future topics, send an e-mail to: NHGRILANDSCAPE@MAIL.NIH.GOV~
~To access past editions, see: genome.gov/2754196~

Rare Disease Research at NHGRI: Not So Rare

Every year in late February, there is a date designated as Rare Disease Day. The goal of this annual event is to raise awareness about rare diseases and the lives they impact. Just last week, NIH held its annual symposium for Rare Disease Day; the archived webcast is accessible here. A rare disease is defined as a disorder or condition affecting fewer than 200,000 people in the United States. However, as it is often said, rare diseases considered together are not so rare! Over 7,000 rare diseases have been identified, with upwards of 25 million people affected by rare diseases in the United States alone— similar to the number of people affected by diabetes.

The small affected population size per disease creates challenges for studying these disorders in several ways. First, it can be difficult to identify patients affected with a particular rare disease, stymying efforts to carry out sufficiently large scientific studies, including clinical trials of treatment response. Even when patients are identified, their locations are often highly dispersed, incurring major costs for their travel to sites conducting appropriate studies. In addition, there is often a lack of adequate incentives for pharmaceutical companies to develop treatments for conditions affecting very small numbers of people, especially with the typical large cost of drug development. Currently, it is estimated that there is a treatment for less than 5% of rare diseases.

One of the features of the NIH Intramural Research Program is that it provides a highly productive environment for studying rare diseases, and this has, in turn, attracted a remarkable set of rare disease experts. For example, NIH intramural researchers are currently studying over 500 rare diseases (involving nearly 2,250 patients) at the NIH Clinical Center.

Within the NHGRI Intramural Research Program, investigators are collectively conducting research on over 45 rare diseases. With the available dedicated clinical resources, physician-scientists can become experts about a particular rare disease within just a few years. Different approaches are used to address different areas of studying rare diseases. The Undiagnosed Diseases Program, headed by NHGRI Clinical Director Dr. William Gahl, combines genome sequencing with the expertise of a network of medical specialists to diagnose the most challenging and rare genetic

New Secretary of Health and Human Services

Dr. Thomas E. Price was sworn in as the 23rd Secretary of Health and Human Services (HHS) on February 10, 2017. Dr. Price received his Bachelor and Doctor of Medicine degrees from the University of Michigan. Most recently, he served as the U.S. Representative for Georgia's 6th Congressional District. In a recent message to employees of the Department of Health and Human Services, Dr. Price affirmed his desire to "… ensure our nation remains the leader in developing innovative health care treatments and solutions while preventing, containing, and curing illnesses that confront communities at home and around the world." For more information about the new HHS Secretary, see hhs.gov/about/leadership/secretary/thomas-e-price-md.

UDN Publishes Framework for Diagnosing Rare Diseases

The Undiagnosed Diseases Network (UDN) is a national research consortium funded by the NIH Common Fund, and is geared towards solving the most challenging medical mysteries through a collaborative network of investigators. Hot off the press is UDN's first publication, which outlines the Network's goals and insights for how best to diagnose ultra-rare medical cases. The paper provides a framework for how other medical centers can use UDN's expertise for their own hard-to-diagnose cases. For additional information, see genome.gov/27567665.

diseases. This program began in-house at NHGRI and NIH, and was later expanded into a national effort, the NIH Undiagnosed Diseases Network. This Network is now routinely making major discoveries about new rare diseases through the intense study of individual patients and families.

Other approaches are also used by NHGRI researchers to study rare diseases. The Institute houses experts in all aspects of clinical research, including the natural history of rare diseases. Elucidating natural histories can be critical to the design of successful clinical trials. Dr. Wendy Introne, a rare disease researcher at NHGRI, conducts clinical research on alkaptonuria, a metabolic disorder occurring in ~1 in 500,000, and Chediak-Higashi disease, a multi-system disease occurring in ~1 in 1,000,000. She began her research on alkaptonuria by defining the natural history of the disorder, with an eye towards investigating a possible therapy.

Dr. Introne credits the unique environment at NIH and its capacity to bring patients from all over the world for comprehensive and state-of-the-art clinical evaluations in a time-efficient manner. “For studying rare diseases, it is critical to gather as large a cohort as possible to fully understand the spectrum of disease and clinical, molecular, and cell biological variability. The NIH is the master of translational medicine.”

By studying rare diseases, discoveries and insights are made about common diseases. For example, Dr. Introne’s studies of the pathophysiology of alkaptonuria have shown that these patients suffer from both arthritis that resembles osteoarthritis and aortic stenosis that resembles more generalized heart-valve disease, such as that seen in the general population. The earlier onset and faster progression of these conditions in alkaptonuria patients distinguish this rare disease from its more common counterparts, but understanding the mechanisms of rare diseases can inform studies of the biological pathways involved in more common disorders.

All major aspects of studying rare diseases can be found within the NHGRI Intramural Research Program. Appropriately, some of the Institute’s research in rare diseases were showcased in a recent Reddit “Ask Me Anything” with experts from the Undiagnosed Diseases Network, including NHGRI’s Dr. William

ENCODE Team ‘Spills All’

Investigators involved in NHGRI’s Encyclopedia of DNA Elements (ENCODE) Project have spent over a decade cataloging genes and candidate functional elements in the human genome. To mark the recent launch of a new phase of ENCODE (see announcement), the Project’s extramural program directors and ENCODE researchers from UCSF participated in a Reddit “Ask Me Anything.” The group fielded over fifty questions on topics ranging from technical and scientific aspects of the project, to favorite aspects of their jobs, to training opportunities at NIH. This event hit Reddit’s front page, coming in at number 24! To see the transcript, visit reddit.com/r/science/comments/5szvl4/.

Guide to Interpreting Genomic Reports: A Genomics Toolkit

The Practitioner Education Working Group of the NHGRI Clinical Sequencing Exploratory Research (CSER) consortium has developed a web-based guide for non-genetics practitioners to understand and use results from genomic tests, such as whole-genome and whole-exome sequencing, in patient care. The guide is designed to help healthcare professionals navigate, and better understand, different parts of genomic test reports. To access the guide, see ashg.org/education/csertoolkit/index.html.

Gahl and Dr. Cyndi Tifft, who discussed everything from diagnosing medical mysteries to getting support when dealing with a loved one with a rare disease. To learn more about rare diseases, visit the NHGRI- and NCATS-funded resource, the Genetic and Rare Diseases Information Center (GARD) at rarediseases.info.nih.gov.

Genomics Research

Designer Compound May Untangle Damage Leading to Some Dementias

Induced Pluripotent Stem Cells Don't Increase Genetic Mutations

NIH Study Reveals How Melanoma Spreads

Diabetes in Your DNA? Scientists Zero in on the Genetic Signature of Risk

Rare Disease Research May Provide Insights into Common Diseases

Notable Accomplishments in Genomic Medicine

NIH and USDA Scientists Publish Goat Genome Sequence

Funding News

NIH Single IRB Policy FAQs for Extramural Community

NHGRI Participation in Development of Highly Innovative Tools and Technology for Analysis of Single Cells (STTR) (R41/R42) and (SBIR) (R43/R44)

Registration Open for Spring 2017 NIH Regional Seminar on Funding & Grants - New Orleans, Louisiana

New Videos

eMERGE & CSER: The Convergence of Genomics and Medicine Meeting

National Advisory Council for Human Genome Research – Feb 2017

The Future of Genetic Codes and BRAIN Codes – George Church

JHU/NHGRI Genetic Counseling Training Program

Availability of Peer Review Videos for Applicants

Request for Information

Processes for Database of Genotypes and Phenotypes (dbGaP) Data Submission, Access, and Management

NIH & NHGRI News

Open for Applications: 2017 NHGRI Short Course in Genomics for Middle/High School and Community College/Tribal College Faculty

New Email Updates on the Latest NHGRI Science, Research, News, Upcoming Events, & Website

NHGRI Funding Opportunities Email List

Unlocking Life's Code: February 2017 Newsletter

Dara Richardson-Heron Named Chief Engagement Officer of the *All of Us*℠ Research Program

---